THE RELATIVE TOXICITY OF NICOTINE SULFATE AND NICOTINIUM COMPOUNDS

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The toxicity of nicotine to insects has been investigated by many workers whose findings have been well summarized by Shepard (1939). As far as chemical structure and toxicity are concerned, only those compounds in which the nicotine molecule was changed very slightly approached nicotine in toxicity. The Eastern Regional Research Laboratory of the U. S. Department of Agriculture has prepared a series of nicotine compounds by addition of radicals to the nitrogen in both the pyrrolidine and pyridine rings. These compounds offered an opportunity to study the effect of such additions on the toxicity of nicotine, and further to correlate chemical structure with toxicity.

Preliminary tests reported by Mayer, Weil, Saunders and Woodward (1947) showed that several of these compounds were more toxic than nicotine in tests on several insects.

Materials

All chemicals used, with the exception of the nicotine sulfate standard, were prepared in the Eastern Regional Research Laboratory. Structural formulae, empirical formulae, molecular weight, percentage of nicotine and information on solubility were furnished for all the compounds.

Alkyl, aralkyl, dialkyl, and diaralkyl nicotinium salts were prepared by methods described by Mayer, Weil, Saunders and Woodward (1947). Mixed nicotinium and hydrogen iodide salts were prepared by neutralizing the pyrrolidine nitrogen of the nicotine with hydrogen iodide leaving the nitrogen in the pyridine ring free to react with alkyl or aralkyl halides to form the corresponding quaternary nicotinium salt.

Attempts were made to prepare 2,4-dinitrophenylnicotinium salts by reacting 2,4-dinitrophenyl halides with nicotine, but under the conditions employed the reaction product decomposed. The reaction of aliphatic acid esters of 2,4-dinitrophenol with nicotine yielded a product which on examination proved to be nicotine 2,4-dinitrophenolate. Toxicity data on the latter compound (ERL-100a) were obtained and are included with those of the nicotinium salts.

Methods

The nicotinium compounds were tested as contact insecticides by spraying on the aphid, *Aphis rumicis* Linn, reared on nasturtium in the greenhouse. All dilutions were made on the basis of nicotine content. The water-soluble nicotiniums were dissolved directly in distilled water and compared in toxicity with nicotine sulfate in the same medium. Compounds not soluble in water were dissolved in acetone (10 ml.) and the acetone solution added to distilled water to make up 150 ml. of spray solution. A similar proportion of acetone was added to the nicotine sulfate standard. Preliminary tests showed that many of the nicotiniums were much less toxic than nicotine sulfate. Therefore, the nicotine content of the sprays using nicotinium compounds was double that of nicotine sulfate in order to avoid extrapolation in

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comparisons of toxicity. No wetting or conditioning agents were added to any of the materials.

The sprayer was designed after Hoskins as described by Richardson (Campbell & Moulton, 1943). As described, this sprayer was built for testing petroleum sprays on houseflies. Addition of a hinged plate under the outlet made it possible to spray the lower sides of nasturtium leaves with the aphids in place. Stems of the sprayed leaves were placed in water and were kept 24 hours in a conditioned room at 80° F. and 60 per cent relative humidity. Counts were made on the basis of movement, that is, any aphid that moved when disturbed by a needle was counted as alive.

The dosage series was applied by varying the spray time. For this series spray times of 5, 10, 20 and 40 seconds were used. Two replicates of each material were made, and the average mortality determined by averaging the percentages killed. If for any reason the two replicates were not consistent, further tests were made of the same materials.

Because of variations in the susceptibility of test insects to spray materials, a nicotine sulfate standard was applied with each series of nicotinium compounds. In reporting the results, these standard sprays have been included with the series with which they were compared.

Results

A summary of the results is given in Table 51. Dosage-response curves were plotted from these data, using logarithmic probability paper and fitting the curves by eye. Since there was usually no question as to the relative toxicity of the nicotiniums and nicotine sulfate, no statistical analysis was made. The relative toxicity was interpolated from the dosage-response curves, using as a dosage unit the concentration times the spray time. Since this led to complex numbers, a dosage of 1 was assigned to .04 per cent nicotine sprayed for 40 seconds. An estimate of relative slope was made, again by observation. All these results have been summarized in Table 52. In general, the results were very consistent. The amount of nicotine in the form of nicotine sulfate required varied greatly in only a few cases. In the tests with *p*-nitrobenzylnicotinium thiocyanate, for instance, one spraying with nicotine sulfate was relatively ineffective. A similar instance occurred in one test with *p*-nitrobenzylnicotinium palmitate. The variation in effectiveness of the nicotiniums in these two series was much less than the variation in potency of nicotine sulfate. For this reason the tests in which large quantities of nicotine sulfate were required have been given very little emphasis.

It will be noted at the outset that only a few of the nicotinium compounds were as toxic as nicotine sulfate. The more effective were Nos. 100a, nicotine 2, 4-dinitrophenolate; and 104, 1 benzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride. Three other materials were less toxic than nicotine sulfate at the levels used, but had steeper dosage-response curves and would be expected to be more toxic than nicotine sulfate at higher dosages. These were Nos. 79, dodecylnicotinium thiocyanate; 94, didodecylnicotinium dithiocyanate, and 138, ethylnicotinium iodide. With regard to slope, 100a also appeared to have a steeper slope than nicotine sulfate. In addition to these materials which approached the toxicity of nicotine sulfate, two others had slopes apparently steeper than nicotine sulfate: 116, dilaurylnicotinium dipicrate and 35, hexadecylnicotinium thiocyanate. However, these materials required so high a dose for equal control as compared with nicotine sulfate that the steeper slope was of little advantage.

TABLE 51. AVERAGE PER CENT KILLED—TWO REPLICATES—SPRAY TIME

Materials	% Nicotine	5 secs.	10 secs.	20 secs.	40 secs.
ERL 36	.08	33.7	39.6	69.5	66.3
37	.08	29.3	38.9	55.7	66.5
53	.08	29.8	27.3	54.7	68.0
55	.08	33.2	44.8	51.4	59.4
58	.08	48.1	54.4	61.1	67.7
90	.08	20.0	20.8	23.7	31.1
Nicotine sulfate	.04	45.5	64.4	75.2	82.4
ERL 99	.08	3.7	5.6	8.4	15.1
106	.08	6.7	8.1	10.8	15.2
107	.08	9.6	16.8	26.1	37.9
108	.08	34.3	35.9	49.2	55.9
109	.08	26.1	47.5	35.9	49.7
110	.08	25.3	44.6	44.4	52.5
Nicotine sulfate	.04	38.4	57.4	57.2	73.2
ERL 118	.08	3.4	4.0	12.4	28.0
121	.08	1.6	4.1	12.1	14.2
119	.08	2.7	8.2	16.5	24.1
122	.08	28.4	30.9	36.1	52.2
120	.08	22.2	32.0	37.8	41.0
143	.08	2.9	14.1	14.9	24.2
144	.08	3.8	6.1	7.8	15.7
Nicotine sulfate	.04	27.1	31.4	61.9	76.8
ERL 105	.08	12.3	18.6	17.9	34.3
103	.08	11.1	14.0	15.9	30.1
104	.08	41.9	61.3	60.0	69.3
102	.08	12.2	15.3	18.4	26.1
Nicotine sulfate	.04	37.6	40.1	51.9	62.8
ERL 100a	.08	63.1	68.8	81.1	90.0
79	.08	27.6	46.9	71.9	78.8
81	.08	30.0	61.5	67.9	77.4
36	.08	22.5	33.0	41.1	52.5
55	.08	41.1	44.5	52.8	61.6
Nicotine sulfate	.04	43.7	52.9	63.9	73.8
ERL 34	.08	39.9	50.0	43.3	66.6
35	.08	22.6	36.2	32.3	71.3
54	.08	31.9	28.7	52.3	57.8
93	.08	11.7	13.0	25.3	28.3
Nicotine sulfate	.04	57.7	66.0	81.9	82.7
ERL 96	.08	17.8	27.5	42.5	43.0
97	.08	14.9	24.9	48.7	69.0
Nicotine sulfate	.04	49.7	52.7	68.2	83.9
ERL 75	.08	35.0	46.4	50.3	61.9
84	.08	35.7	45.7	53.6	58.7
85	.08	13.5	12.2	19.6	17.4
86	.08	40.9	44.5	52.8	57.8
87	.08	12.9	25.4	34.4	41.5
Nicotine sulfate	.04	52.1	64.9	72.9	78.2
ERL 73	.08	14.0	22.5	26.3	25.9
76	.08	48.2	67.3	70.8	76.5
31	.08	33.9	45.2	58.6	64.5
72	.08	57.1	58.8	57.5	69.0
Nicotine sulfate	.04	61.1	61.2	71.1	79.4

Table 51. Average Per Cent Killed—Two Replicates—Spray Time (cont'd)

Materials	% Nicotine	5 secs.	10 secs.	20 secs.	40 secs.
ERL 79	.08	19.5	24.5	56.3	68.8
Nicotine sulfate	.04	76.7	75.6	77.7	79.3
ERL 30	.08	12.0	10.9	14.4	17.5
52	.08	43.9	52.1	60.6	74.6
74	.08	35.3	57.9	43.0	83.7
Nicotine sulfate	.04	37.6	32.3	41.8	68.6
ERL 30	.08	23.9	31.9	28.6	40.6
52	.08	68.2	65.5	80.2	81.3
74	.08	27.3	47.2	45.2	62.6
88	.08	57.3	70.7	73.8	82.9
89	.08	31.8	37.9	42.5	51.0
Nicotine sulfate	.04	65.6	81.0	78.6	81.4
ERL 79	.08	27.3	30.9	37.9	73.9
81	.08	23.1	53.2	57.5	65.0
82	.08	47.8	57.2	57.3	71.4
83	.08	48.1	72.7	74.0	80.8
98	.08	38.6	45.3	64.5	68.9
Nicotine sulfate	.04	65.7	65.5	74.6	82.5
ERL 29	.08	44.2	41.6	56.7	52.5
51	.08	34.8	35.8	64.7	67.5
56	.08	38.1	57.7	60.7	76.5
57	.08	46.0	65.1	74.0	84.0
Nioctine sulfate	.04	55.7	65.0	76.8	77.9
ERL 91	.08	11.0	15.5	12.8	39.6
94	.08	28.9	42.6	57.8	76.9
115	.08	28.5	48.8	32.7	29.7
116	.08	11.6	19.0	47.1	55.6
117	.08	15.3	27.3	29.4	35.1
Nicotine sulfate	.04	42.5	61.1	61.5	73.4
ERL 91	.08	14.4	14.2	22.9	
94	.08	16.4	30.4	63.0	
74	.08	25.5	36.3	45.0	
51	.08	42.3	45.6	41.1	
56	.08	25.0	32.6	45.7	
57	.08	34.6	39.9	50.0	
Nicotine sulfate	.04	36.0	45.2	58.1	
ERL 80	.08	15.8	28.6	35.4	[illegible]
92	.08	5.6	9.9	14.3	1
139	.08	13.1	11.5	23.2	3
141	.08	11.4	17.0	15.1	2.
77	.08	9.2	20.4	23.0	3
78	.08	21.8	31.9	35.3	54
140	.08	11.5	11.8	12.8	15.
142	.08	12.3	13.4	25.8	27.
Nicotine sulfate	.04	24.6	38.2	46.2	65.
ERL 111	.08	24.7	37.4	42.6	59.2
112	.08	53.3	50.4	55.5	63.4
113	.08	40.1	39.4	43.7	52.2
114	.08	25.6	46.7	50.8	56.0
137	.08	11.7	9.9	21.2	28.0
138	.08	27.9	36.2	51.7	76.1
Nicotine sulfate	.04	39.4	56.5	60.3	73.7

TABLE 52. COMPARISON OF TOXICITY OF NICOTINIUM COMPOUNDS AND NICOTINE SULFATE

ERL No.	Compound	Per cent killed at level of comparison	Dosage required: ERL	Dosage required: Nicotine sulfate	Toxicity of ERL[1]	Slope[2]
107	methylnicotinium bromide	40	1.7	.13	8	parallel
108	ethylnicotinium bromide	50	1.0	.2	20	flat
80	butylnicotinium bromide	40	.9	.2	22	parallel
81	dodecylnicotinium bromide	70	1.0	.6	60	parallel
			2.0	.2	10	parallel
34	hexadecylnicotinium bromide	70	2.1	.2	10	parallel
36	octadecylnicotinium bromide	50	1.4	.15	10	parallel
			1.5	.3	20	parallel
72	benzylnicotinium bromide	60	.7	.11	16	flat
31	o-chlorobenzylnicotinium bromide	70	2.0	.2	10	parallel
30	*p*-nitrobenzylnicotinium bromide	50	5.0	.1	2	flat
			6.0	.1	1.7	flat
111	1,2-ethylene-bis (nicotinium bromide)	60	1.9	.3	16	parallel
112	poly(2-bromoethylnicotinium bromide)	60	1.0	.3	33	flat
106	dimethylnicotinium dibromide	Less than			1	flat
109	diethylnicotinium dibromide	50	1.0	.2	20	flat
92	dibutylnicotinium dibromide	40	9.0	.2	2	parallel
91	didodecylnicotinium dibromide	40	3.0	.15	5	parallel
73	dibenzylnicotinium dibromide	60	>10.0	.1	<1	flat
93	methylnicotinium iodide	60	15.0	.1	.6	parallel
138	ethylnicotinium iodide	60	.8	.27	34	steep
139	butylnicotinium iodide	40	1.7	.22	13	parallel
140	octylnicotinium iodide	40	3.0	.22	7	flat
141	dodecylnicotinium iodide	40	1.0	.22	22	parallel
142	octadecylnicotinium iodide	40	>100	.22	< .1	parallel
90	dimethylnicotinium diiodide	50	> 10	.1	<1	flat
105	1-methyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium iodide	40	2.8	.15	5	parallel
137	diethylnicotinium diiodide	50	10	.13	1.3	parallel

TABLE 52. COMPARISON OF TOXICITY OF NICOTINIUM COMPOUNDS AND NICOTINE SULFATE (cont'd)

ERL No.	Compound	Per cent killed at level of comparison	Dosage required		Toxicity of ERL[1]	Slope[2]
			ERL	Nicotine sulfate		
98	dodecylnicotinium chloride	70	1.4	.2	16	parallel
29	benzylnicotinium chloride	60	3.0	.13	4	flat
84	*p*-chlorobenzylnicotinium chloride	60	2.5	.15	6	flat
86	2,4-dichlorobenzylnicotinium chloride	60	2.5	.15	6	flat
88	3,4-dichlorobenzylnicotinium chloride	80	1.0	.45	45	flat
113	2,2/-bis(nicotinium chloride) ethyl ether	50	1.5	.15	10	flat
114	poly[2-(2-chloroethoxy) ethylnicotinium chloride]	60	2.0	.27	13	parallel
104	1-benzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride	70	1.2	1.5	125	parallel
103	1-*p*-chlorobenzyl-3[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride	40	7.0	.15	2	parallel
102	1-*p*-nitrobenzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride	40	10.0	.15	1.5	flat
96	didodecylnicotinium dichloride	60	2.4	.2	8	parallel
85	di-*p*-chlorobenzylnicotinium dichloride	60	>100	.15	<1	flat
87	di-2,4-dichlorobenzylnicotinium dichloride	60	4.0	.15	4	parallel
89	di-3,4-dichlorobenzylnicotinium dichloride	50	1.5	.1	6	flat
78	butylnicotinium thiocyanate	40	.7	.2	30	parallel
77	octylnicotinium thiocyanate	40	1.8	.2	11	parallel
35	hexadecylnicotinium thiocyanate	70	2.1	.2	10	steep
37	octadecylnicotinium thiocyanate	70	1.5	.3	20	parallel
79	dodecylnicotinium thiocyanate	70	.8	.6	75	steep
		60	1.0	.1	10	steep
76	benzylnicotinium thiocyanate	70	.7	.3	43	parallel
75	o-chlorobenzylnicotinium thiocyanate	60	1.5	.15	10	flat
74	*p*-nitrobenzylnicotinium thiocyanate	60	1.5	.35	23	parallel
		60	1.3	.15	11	parallel
94	didodecylnicotinium dithiocyanate	60	.75	.35	46	steep
143	butylnicotinium *p*-toluenesulfonate	30	2.7	.13	5	flat
121	2-methyl-2-propen-1-ylnicotinium *p*-toluenesulfonate	30	3.5	.13	4	flat
120	allylnicotinium *p*-toluenesulfonate	30	.3	.13	43	flat

Table 52. Comparison of Toxicity of Nicotinium Compounds and Nicotine Sulfate (cont'd)

ERL No.	Compound	Per cent killed at level of comparison	Dosage required ERL	Dosage required Nicotine sulfate	Toxicity of ERL[1]	Slope[2]
122	2-chloro-2-propen-1-ylnicotinium *p*-toluenesulfonate	30	.25	.13	52	flat
118	2,2′-bis(nicotinium *p*-toluenesulfonate) ethyl ether	30	1.5	.13	9	parallel
119	2-nicotinium *p*-toluenesulfonate-2′-(2-nicotinium *p*-toluenesulfonate ethoxy) ethyl ether	30	1.9	.13	7	parallel
144	2-(2-butoxy-ethoxy) ethylnicotinium *p*-toluenesulfonate	30	6.0	.13	2	flat
56	benzylnicotinium palmitate	70	1.3	.3	23	parallel
52	*p*-nitrobenzylnicotinium palmitate	70	2.0	.3	15	parallel
		80	1.0	.45	45	flat
		70	1.4	1.2	90	parallel
82	dodecylnicotinium propionate	70	2.0	.2	10	parallel
100a	nicotine 2,4-dinitrophenolate	80	.9	1.5	167	steep
83	dodecylnicotinium oleate	70	.6	.2	30	parallel
		60	2.0	.15	7	parallel
51	benzylnicotinium oleate	60	4.5	.45	10	flat
97	didodecylnicotinium dioleate	60	1.7	.2	12	parallel
54	methylnicotinium stearate	60	2.0	.1	5	
57	benzylnicotinium stearate	70	.7	.3	43	parallel
115	dodecylnicotinium picrate	50	2.5	.13	5	flat
117	3-[2-(1-dodecyl-1-methylpyrrolidyl bromide)] pyridine picrate	50	3.5	.13	4	parallel
116	didodecylnicotininum dipicrate	50	1.1	.13	12	steep
53	octadecylnicotinium acetate	70	2.0	.3	15	flat
99	dioctadecylnicotinium diacetate	Less than			1	flat
55	octadecylnicotinium laurate	60	2.2	.17	8	flat
58	octadecylnicotinium valerate	70	2.0	.3	15	parallel
110	methylnicotinium methylsulfate	50	1.0	.2	20	flat

1 On the basis of dosage of nicotine sulfate equalling 100 per cent.
2 Slope of dosage-response curve in relation to nicotine sulfate.

Dimond et al. (1941) have shown that slope may be affected (1) by the organism used (2) by the age and nutrition of the organism (3) by the toxicant and (4) by coverage. The same organism was used in all these tests and since the aphids were selected at random the age and nutrition should not be a factor. The method used in these tests did not control coverage, since there was no attempt to control the surface tension of the spray mixtures. It is, therefore, impossible to determine whether the differences in slope were caused by changes in the toxicant or by coverage. Probably both were involved. It does seem worth noting that all of the highly toxic nicotiniums had slopes apparently steeper than the slope of the nicotine sulfate standard.

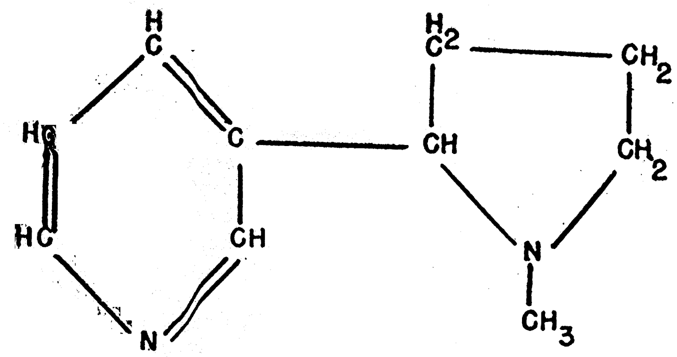
A large group of compounds had dosage-response curves with slopes definitely flatter than for nicotine sulfate. Few of these compounds were very toxic, and obviously the toxicity in comparison with nicotine sulfate decreased as the dosage was increased. If these slopes are any definite indication of changes in the mode of action of the nicotiniums, there are not enough correlations to establish any relationship between chemical structure and slope. Likewise, there appears to be no definite relationship between wetting properties and slope. For instance, octadecylnicotinium thiocyanate, with a contact angle of 50, had a much flatter slope than the cetylnicotinium thiocyanate with a contact angle of 52.

In spite of the fact that none of these compounds was promising as a replacement for nicotine sulfate, it is of interest to examine the data critically in an attempt to determine reasons for differences in toxicity between nicotine sulfate and the nicotinium compounds, and between the various nicotiniums.

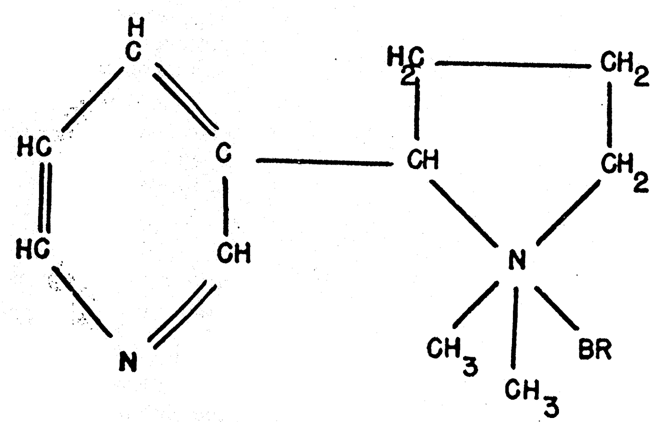
Richardson, Craig and Hansberry (1936) have shown that the substitution of a hydrogen atom for the methyl group on the nitrogen of the pyrrolidine ring did not change the toxicity of the compound. The substitution of a piperidine ring (in anabasine) for the pyrrolidine ring increased toxicity sharply. Campbell, Sullivan and Smith (1933) have reported that the substitution of a methyl group for the hydrogen in the piperidine ring of anabasine reduces the toxicity slightly. Richardson and Shepard (1930) showed that breaking the pyrrolidine ring reduced the toxicity sharply.

In the present study the modification in the nicotine molecule was additive on the nitrogen in the two rings. The simplest change made was the direct addition of an alkyl halide to the trivalent nitrogen in the pyrrolidine ring, forming a quaternary ammonium salt. (See Fig. 12). When such an addition was made, the toxicity of the compound was reduced sharply. Thus No. 107, methylnicotinium bromide was only 8 per cent as toxic as nicotine. When an additional alkyl halide was added to the nitrogen in the pyridine ring (See Fig. 12), the toxicity was still further reduced, as in No. 106, dimethylnicotinium dibromide, which was less than 1 per cent as toxic as nicotine sulfate. Within this series of compounds there were 11 comparisons between mono- and di-substituted nicotiniums. In nine instances the di-substituted compounds were definitely less toxic than the mono-. Dodecyl nicotinium thiocyanate was tested twice—in one test it was more toxic than didodecyl nicotinium dithiocyanate and in the other test less toxic. Dodecyl nicotinium picrate was also less toxic than dilaurylnicotinium dipicrate.

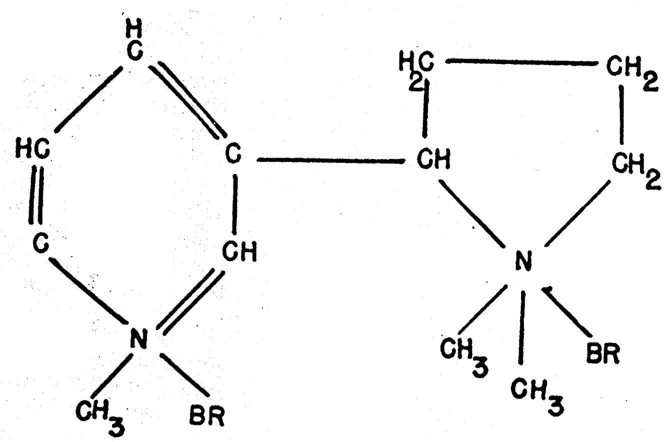
The combination of nicotinium and hydrogen iodide salts in the same molecule in general fails to produce any substantial toxicity. Thus 1-methyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium iodide shows only a slight increase in toxicity over either the methylnicotinium iodide or dimethylnico-



NICOTINE



METHYL NICOTINIUM BROMIDE



DIMETHYL NICOTINIUM DIBROMIDE

Figure 12

tinium diiodide. Similarly 1-*p*-nitrobenzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride and the *p*-chlorobenzyl form of the same compound show relatively low toxicity.

On the other hand, 1-benzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride, which differs from the latter two compounds only in the absence of a substituent on the benzyl group, was more toxic than nicotine sulfate.

Since in most cases addition of radicals to the pyrrolidyl nitrogen reduced toxicity and addition to the pyridine nitrogen reduced toxicity still more, it seems logical to conclude that the two nitrogens are very important to the toxicity of nicotine.

In spite of the fact that additions to nicotine reduced toxicity, the compounds varied in potency. In the bromides, toxicity increased from methyl to dodecyl, and then decreased as the length of the radical was increased further. In the iodides there was a less regular increase in potency and the ethyl nicotinium iodide was the most toxic of the series. In the thiocyanates dodecyl was again the most toxic of the series. This relationship agrees well with the results of Siegler and Popenoe (1942) and Tattersfield and Gimingham (1927). In other words the toxicity of these nicotiniums seemed to be controlled more by the nature of the added radicals than by the fact that the nicotine molecule was present.

Substitution of the benzyl radical for a straight chain had a variable effect. In the thiocyanates the benzyl was slightly more toxic than dodecyl. In the chlorides, bromides and oleates the benzyl was much less toxic than the dodecyl compounds. Substitution on the benzene ring also affected toxicity. O-chlorobenzylnicotinium thiocyanate was less toxic than benzylnicotinium thiocyanate, and the same was true of the bromides. *p*-Chlorobenzylnicotinium chloride was less toxic than the benzyl compound. 2,4-dichlorobenzylnicotinium chloride was also less toxic than benzyl. The 3,4 compound was one of the most toxic chlorides tested, however.

p-Nitrobenzylnicotinium bromide was less toxic than the benzyl bromide. In the thiocyanates and palmitates, *p*-nitrobenzyl was more toxic than benzyl.

Nicotine 2,4-dinitrophenolate (not a nicotinium) was the most toxic compound tested. Tattersfield et al. (1925) have shown that 2,4-dinitro compounds are highly toxic to insects.

Synthesis of compounds containing two molecules of nicotine such as 2,2′-Bis(nicotinium chloride) ethyl ether did not produce high toxicity. In fact, these molecules were less toxic than some of the smaller and simpler compounds.

Although the series of compounds available for comparison is not large, it seems that in general the iodides were less toxic than the corresponding bromides. Two of the chlorides were less toxic than the similar bromides, while one was slightly more toxic. The thiocyanates were much more toxic than the halogen compounds. The propionates, oleates, stearates, palmitates, laurates, valerates and *p*-toluene sulfonates were certainly not outstanding in toxicity. The acetates, picrates and sulfates were also mediocre.

The toxicity of the nicotine molecule was certainly not dominant in the nicotiniums. It did influence toxicity, however, as illustrated by comparing dodecylnicotinium thiocyanate with dodecylisoquinolinium thiocyanate, with the following results:

Material	Mortality at spray time—seconds 5	10	20	40
Dodecylnicotinium thiocyanate	19.5	24.5	56.3	68.8
Dodecylisoquinolinium thiocyanate	13.7	13.3	17.0	17.4

Obviously the dodecyl and thiocyanate radicals on these two compounds did not produce equal toxicity. Equally obviously one striking difference between nicotine and isoquinoline is the single nitrogen in isoquinoline. This seems to offer additional evidence of the importance of the two nitrogens in the toxicity of nicotine.

Relation Between Physical Properties and Toxicity

The nicotinium compounds differ from nicotine sulfate in physical properties as well as in chemistry. The physical properties are, of course, established by the components of the molecule. It is of interest to examine the more obvious physical properties for their relationship to toxicity.

Solubility

Most of the nicotinium compounds were soluble in water at the concentrations used in this series of tests. In a few cases it was possible to compare the toxicity of water-insoluble compounds with closely related water-soluble materials. Water-insoluble benzyl nicotinium thiocyanate was more toxic than soluble butyl, octyl, cetyl and octadecyl thiocyanates, and probably more toxic than dodecylnicotinium thiocyanate. On the other hand, the two most toxic nicotiniums were water soluble. While solubility in water may have some bearing on toxicity, it appears to be considerably less important than structure of the molecule.

Wetting Properties and Toxicity

Unquestionably the wetting properties of a spray have much to do with its toxicity as a contact insecticide. Contact angles of several nicotiniums

TABLE 53. CONTACT ANGLE AND TOXICITY OF NICOTINIUM COMPOUNDS

ERL No.	Material	Contact angle degrees[1]	Toxicity rating (Table 52)
75	o-chlorobenzylnicotinium thiocyanate	100	10
77	octylnicotinium thiocyanate	100	11
78	butylnicotinium thiocyanate	97	30
74	*p*-nitrobenzylnicotinium thiocyanate	99	23
			11
			109
76	benzylnicotinium thiocyanate	100	43
79	dodecylnicotinium thiocyanate	41	75
			6
37	octadecylnicotinium thiocyanate	50	20
52	hexadecylnicotinium thiocyanate	52	10
72	benzylnicotinium bromide	100	16
73	dibenzylnicotinium dibromide	100	>1
31	o-chlorobenzylnicotinium bromide	90	10
80	butylnicotinium bromide	96	22
30	*p*-nitrobenzylnicotinium bromide	67	2
81	dodecylnicotinium bromide	59	60
			10

[1] water = 100, angles given as per cent of the angle of water.

dissolved in water have been made available by Howard[1]. The comparative toxicity and contact angle are given in Table 53. It is obvious that there was no correlation between contact angle of these materials and their toxicity. Possibly poor wetting properties may have been responsible for the low toxicity of some compounds. However, closely related materials which did reduce the contact angle were not substantially more toxic.

Summary

The toxicity of a group of nicotinium compounds as contact insecticides has been determined by spraying on *Aphis rumicis* using nicotine sulfate as a standard.

Only 1-benzyl-3-[2-(1-methylpyrrolidyl-hydriodide)] pyridinium chloride exceeded the toxicity of nicotine sulfate.

Reduction of toxicity by addition of radicals to the nitrogen in the pyrrolidine ring, and further reduction by addition to the nitrogen in the pyridine ring suggests that these nitrogens are very important in the toxicity of nicotine. Adding radicals to them reduced the toxicity of nicotine as much as breaking the pyrrolidine ring as reported by Richardson and Shepard (1930).

The most toxic nicotinium compound (No. 104) produced a dosage-response curve parallel to the curve for nicotine sulfate. Two compounds producing steeper slopes were not highly toxic. The changes in slope could not be correlated with wetting properties.

The relative toxicity of the nicotinium compounds was influenced by the structure of the added radicals. Dodecyl compounds were outstanding in this respect. Substitution of the benzyl radical reduced toxicity and addition of halogens to the benzyl radical reduced toxicity still further.

The nicotine structure had an effect on toxicity, since dodecylnicotinium thiocyanate was much more toxic than dodecylisoquinolinium thiocyanate.

Degree of toxicity was not correlated with solubility in water.

There was no correlation between contact angle and toxicity.

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[1] For permission to use these data, thanks are due to Dr. Frank L. Howard, Plant Pathologist of the Rhode Island Agricultural Experiment Station, Kingston, R. I.

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MISCELLANEOUS INSECT NOTES

Fly Control with DDT

An experimental spraying project was conducted on property located at Brooklyn, Conn., and owned by the Windham County Agricultural Society on September 12, 1946. The day prior to the day on which the spraying was accomplished, the area in the vicinity of a food dispensing booth on the Agricultural Society Fair Grounds at Brooklyn was visited during the late morning hours and in the evening. During the morning visit, an abundance of flies were noted; during the evening visit, numerous mosquitoes were present. The area was sprayed at approximately 9:00 A.M. on September 12 with an emulsion of DDT. The stock emulsion contained two pounds of DDT to one gallon of water and this was diluted to 300 gallons before application. The outside of the food dispensing booth and the ground around the booth (approximately one-half acre) were drenched with the emulsion. On the afternoon of the same day, a visit was made to the area to observe conditions. It was immediately apparent that the fly population was nil. Members of the Department were unable to make further observations themselves, but from information received by the writer from members of the group that operated the food dispensing booth, at no time during the three-day period that the booth was in operation were flies or mosquitoes plentiful enough to cause discomfort or annoyance, even on the third day, at which time the grounds around the food booth had become littered with fragments of foodstuffs.

O. B. Cooke

Control of Carpenter Ants in Telephone Poles

Mr. A. B. Carlson of the Southern New England Telephone Company very kindly has sent us an excerpt from the SNETC pole inspection summary for 1946 by Mr. C. C. Potter.

"Treatment for the control of carpenter ants[1] was administered to 738 poles, (this includes 88 poles which had been treated previously and were retreated this year). This compares with other years since the control measure was adopted as follows:

1938 —	642	1943 —	818
1940 —	807	1944 —	520
1941 —	1,321	1945 —	786
1942 —	1,498	1946 —	738

"Ant activity in 119 other poles was found too serious to control by treatment and they were condemned (this includes 21 poles which had been previously but ineffectually treated).

"A total of 883 poles previously treated for the control of ants was reinspected this year. There were no ants found in 665 or 75 per cent. In the 218 where ants were still present 21 were condemned because of ant damage, 109 condemned for some other defect and 88 retreated."

The above means that only 21 poles (2.4 per cent) out of 883 failed to respond to this treatment.

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1 See Friend and Carlson 1937, Conn. Agr. Exp. Sta. Bul. 403, for a description of this treatment.

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1 Inasmuch as the articles in this Report written by members of the Department all bear the authors' names, they are not listed here.